



ENLIGHTENMENT ON NAEGLERIA FOWLERI; A BRAIN EATING AMOEBA- AN ALARMING CALL

*Syeda Sarah Abbas¹ | Safila Naveed² | Fatima Qamar³ | Zohra Barkat Ali⁴

¹ Faculty of Pharmacy, Jinnah University for women Karachi, *Corresponding Author

^{2,3,4} (Department of Pharmaceutics), Faculty of Pharmacy, University of Karachi

ABSTRACT

Naegleria fowleri is also called as brain eating amoeba. It is a very dangerous and life threatening disorder that cause PAM (primary amebic meningoencephalitis). The ultimate source of *Naegleria* is contaminated water or water with poor chlorine level. It is usually examined under CT scan, PCR and CSF. According to research, there is increasing number of PAM in Karachi, Pakistan. The purpose of this core study or review is to give awareness and provide its better management in the light of different updated new studies

Key words: *Naegleria fowleri*, Primary Amebic Meningoencephalitis (PAM), Brain Eating Amoeba, Karachi, Pakistan.

Introduction:

Naegleria fowleri is a species of kingdom protista which is free living commonly called as brain eating amoeba that can cause unique but disastrous infection known as primary amebic meningoencephalitis (PAM) this infection is also called as Naeglariasis. The amoeba lives in warm fresh water (rivers, lakes) and soil. It is a single celled eukaryotic organism. People usually infected from either contaminated water or not then this water enters in body through nose then *Naegleria* enters in brain that causes PAM.

History:

In Australia 1965 Dr fowler and cutler 1st described the disease caused by amoeba flagellate. He described that amoeba flagellate is a free living organism, lives in both environment in human causing PAM. Almost 144 cases from all over the world identified. Dr Fowler and cutler named this organism *N fowleri*.^(1,2)

Naegleria fowleri life cycle:

There are 3 main stages of *n fowleri* life cycle:

- 1) Trophozoites (feeding)
- 2) Flagellate (motility)
- 3) Cysts (surviving)

In these stages trophozoites stage is an infective stage. During binary fission trophozoites replicate and their nuclear membrane remains intact. Trophozoites infect people and animal when enters through nose (nasal tissue) and then migrate to brain causing primary amebic meningoencephalitis (PAM). Trophozoites found in CSF and as well as in tissue. When there are unfavorable condition trophozoites convert into flagellate and then form cysts. It is resistant and increases the chances of survival⁽³⁾



Figure 1: Life cycle of *Naegleria*

Causing illness:

Naegleria fowleri cause primary amebic meningoencephalitis resulting bleeding.⁽⁴⁾ Primary amebic meningoencephalitis due is hazardous, necrotizing, and hemorrhagic meningoencephalitis, characterized by severe headache, stiff neck, fever (38.5°C–41°C), altered men-

tal status, seizures, and coma, leading to death^(5,6,7,8)

Signs and symptoms:

Sign and symptoms begin after the exposure to *Naegleria* containing water. It is divided into 2 stages.

Stage 1 sign and symptoms: fever, nausea, vomiting and a severe frontal headache. (Mild symptoms)

Stage 2 sign and symptoms: stiff neck, altered mental status, hallucinations, seizures, and coma. (Severe symptoms)⁽⁹⁻¹¹⁾

Epidemiology:

Pakistan is also victim of this disease. 20 deaths reported in Karachi in 2010.⁽¹²⁾ In 2011, 13 more cases reported in Karachi.⁽¹³⁾ In 2014 one more case reported which was very fatal.⁽¹⁴⁾ In April 2015, 5 more deaths occur in Karachi.⁽¹⁵⁾ In May 2015, 4 another cases is reported.⁽¹⁶⁾ According to this research there is increasing number of cases in Karachi.

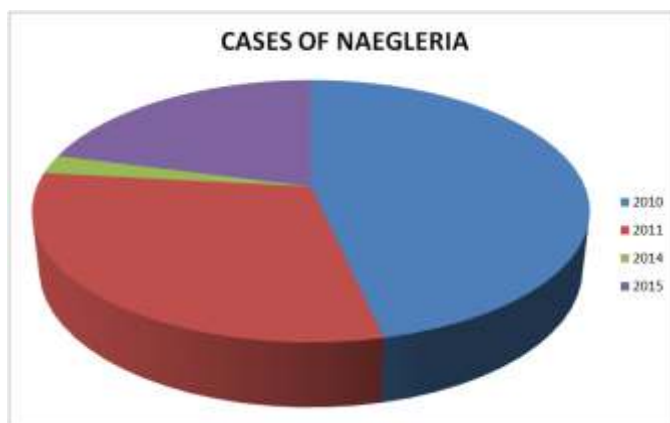


Figure 2: Proportions and incidents of *Naegleria* over the recent years

Diagnosis:

PAM is diagnosed by the help of biopsy, CSF or tissue specimens either organism or nucleic acid of *Naegleria* is detected.

CSF:

A fresh CSF is taken and sediment it but it should be fresh, unrefrigerated, unfrozen, so after sedimentation trophozoites of *Naegleria* seen in microscope. CSF may correlate with degree of inflammation and necrosis present. It may be grayish or yellowish color. In CSF analysis of *Naegleria* patient elevated protein level, elevated neutrophilic pleocytosis, hypoglycorrhachia, GS and LA were negative observed.

PCR:

PCR is used to identify *Naegleria fowleri*. PCR is amplification of DNA. It is a scientific technique in molecular biology. (17, 18) Through PCR trophozoites and cysts of *Naegleria fowleri* is identified.

CT scan:

CT scan is used to identify the structure of brain in *Naegleria fowleri*. It is used to identify either lesions or not.

Treatment:

Drug name	Category	Mechanism of action	Indications	Side effects
Amphotericin B	Antifungal	Bind with sterols of fungal membrane and <i>Naegleria fowleri</i> leads to cell death	Zygomycosis, PAM, systemic candidiasis, coccidioidomycosis, histoplasmosis	Diarrhea, nausea, chills, vomiting, malaise
Rifampicin	Enzyme inhibitors	Inhibits the DNA dependent RNA polymerase leading to cell death.	Mycobacterial infections	Heartburn, nausea, drowsiness, dizziness.
Sulfadiazine	Sulphonamides	Inhibit the bacterial enzyme	Meningococcal meningitis	Nausea, vomiting, diarrhea, headache

IMMUNIZATION AGAINST NAEGLERIA FOWLERI:

Naegleria as we discussed above is the causal agent of PAM in humans. There is no any sign of acquired human immunity in human but mice shows specific antigens that mean mice develop immunization against *N. fowleri*. IgG antibodies detect in ICR mice against *Naegleria fowleri*.^(20,21)

Humoral immunity is not enough so considerable endeavor has been made to show that mice can be immunized through intraperitoneal inoculation of live or dead amoeba by formalin fixation.⁽²²⁾ NFa1 protein immunized intraperitoneally and intra nasally in mice which shows serological response through this response high level of NFa1-specific IgG, including IgG2b, IgG2a and IgG3, and IgA antibodies developed.⁽²³⁾ NFa1 protein immunized in mice against *Naegleria* using mucosal and result shows that there is increase serum level of IgG antibodies in mice infected with PAM due to *Naegleria fowleri*.⁽²⁴⁾ Further more studies also conduct in experimental animals.⁽²⁵⁻²⁷⁾ our research group also did work on a variety of subjects to elevate the level of awareness, alertness and improve the health and well being of the citizen in a society⁽²⁸⁻³⁶⁾

Result and Discussion:

Naegleria fowleri is a hazardous to human life. According to research it is increasing day by day through water contagion. Mild symptoms convert into severe within couple of days. The best way to diagnose *Naegleria* is CSF, PCR and CT scan. Various drugs shows improvement in patients with PAM those medicines are Amphotericin B, Rifampicin and sulfadiazine. According to latest research many immunization test occur in mice and very prompt response against *Naegleria* is identified. Antibodies against *Naegleria* are formed in mice. So by now it can be manageable and curable up to some extent and by proper chlorination of water. The main task behind this collection of latest researches is to tackle this alarming disease and its proper management

REFERENCES

- Butt CG (1966) *Primary amebic meningoencephalitis*. N Engl J Med 274:1473-1476
- Fowler M & Carter RF (1965) *Acute pyogenic meningitis probably due to Acanthamoeba sp.: a preliminary report*. Br Med J 2: 740-742.
- Life Cycle of Naegleria fowleri*. Free-Living Amebic Infections July 20, 2009 [cited 2010 February 26]
- Gautam PL, Sharma S et al. A rare case of survival from primary amebic meningoencephalitis. Indian Crit Care med. 2012 Jan;16(1):34-36. doi: 10.4103/0972-5229.94432.)

- Martinez AJ, Visvesvara GS (1997) Free-living, amphi-zoic and opportunistic amebas. Brain Pathol 97: 583-598. doi: 10.1111/j.1750-3639.1997.tb01076.x
- Visvesvara GS (2010) Free-Living Amebas as Opportunistic Agents of Human Disease. J Neuroparasitology 1 Article ID N100802. doi: 10.4303/jnp/n100802
- Tuppeny M (2011) Primary amebic meningoencephalitis with subsequent organ procurement: a case study. J Neurosci Nurs 43: 274-279. doi: 10.1097/jnn.0b013e318227ef6e
- Trabelsi H, Dendana F, Sellami A, Sellami H, Cheikhrouhou F, et al. (2012) Pathogenic free-living amoebae: epidemiology and clinical review. Pathologie Biologie (Paris) 60: 399-405. doi: 10.1016/j.patbio.2012.03.002
- Rabago D, Zgierska A, Mundt M, Barrett B, Bobula J, et al. (2002) Efficacy of daily hypertonic saline nasal irrigation among patients with sinusitis: A randomized controlled trial. J Fam Pract 51: 1049-1055.
- Rabago D, Zgierska A (2009) Saline nasal irrigation for upper respiratory conditions. Am Fam Physician 80: 1117-1119.
- Rabago D, Pasic T, Zgierska A, Mundt M, Barrett B, et al. (2005) The efficacy of hypertonic saline nasal irrigation for chronic sinonasal symptoms. Otolaryngol Head Neck Surg 133: 3-8. doi: 10.1016/j.otohns.2005.03.002
- Shakoor S, Beg MA, Mahmood SF, et al. Primary amebic meningoencephalitis caused by *Naegleria fowleri*, Karachi, Pakistan. Emerg Infect Dis 2011;17:258-61
- Volume 17, Number 2—February 2011 Primary Amebic Meningoencephalitis Caused by *Naegleria fowleri*, Karachi, Pakistan Sadia Shakoor, Mohammad Asim Beg, Syed Faisal Mahmood, Rebecca Bandea, Rama Sriram, Fatima Noman, Farheen Ali, Govinda S. Visvesvara, and Afia Zafar Author affiliations: Author affiliations: Aga Khan University Hospital, Karachi, Pakistan (S. Shakoor, M.A. Beg, S.F. Mahmood, F. Ali, A. Zafar); Centers for Disease Control and Prevention, Atlanta, Georgia, USA (R. Bandea, R. Sriram, G.S. Visvesvara); Liaquat National Hospital, Karachi (F. Noman))
- (. Shariq A, Afridi FI, Farooqi BJ, Ahmed S, Hussain A. Fatal primary meningoencephalitis caused by *Naegleria fowleri*. J Coll Physicians Surg Pak 2014; 24:523-5.)
Brain-eating amoeba: *Naegleria* claims fifth life in a month
- By Sameer Mandhro Published: May 27, 2015
- Naegleria* Four case (Brain Eating Amoeba) Reported in 2015 in Karachi -Pakistan May 30, 2015)
- POLYMERASE CHAIN REACTION: METHODS, PRINCIPLES AND APPLICATION Dr.Mohini Joshi1*, Dr.Deshpande J.D2.

Department of Anatomy, Rural Medical College, Pravara Institute of Medical Sciences, Loni, Maharashtra, India Department of Community Medicine, Rural Medical College, Pravara Institute of Medical Sciences, Loni, Maharashtra, India

- A real-time PCR diagnostic method for detection of *Naegleria fowleri* ARTICLE in EXPERIMENTAL PARASITOLOGY · NOVEMBER 2009
- Basic & Clinical Pharmacology, 12e Bertram G. Katzung, Susan B. Masters, Anthony J. Trevo
- Park KM, Ryu JS & Im KI. Blastogenic responses of splenic lymphocytes to *Naegleria fowleri* lysates and T-cell mitogen in mice with primary amebic meningoencephalitis. Korean J Parasitol 1987; 25: 1-6.

- 21) Lee SG, Im KI & Lee KT. Protective immunity against *Naegleria meningoencephalitis* in mice. *Korean J Parasitol* 1985; 23:293–299.
- 22) Thong YH, Shepherd C, Ferrante A & Rowan-Kelly B. Protective immunity to *Naegleria fowleri* in experimental amebic meningoencephalitis. *Am J Trop Med Hyg* 1978; 27: 238–240
- 23) Effects of immunization with the rNfa1 protein on experimental *Naegleria fowleri*-PAM mice Y. J. LEE^{1,†}, J. H. KIM^{1,†}, H. J. SOHN¹, J. LEE¹, S. Y. JUNG², Y. J. CHWAE¹, K. KIM¹, S. PARK¹ and H. J. SHIN¹ Article first published online: 15 JUN 2011 DOI: 10.1111/j.1365-3024.2011.01296.x
- 24) 2015 Apr;114(4):1377-85. doi: 10.1007/s00436-015-4316-3. Epub 2015 Jan 22. Protective immunity against *Naegleria fowleri* infection on mice immunized with the rNfa1 protein using mucosal adjuvants. Lee J1, Yoo JK, Sohn HJ, Kang HK, Kim D, Shin HJ, Kim JH
- 25) Bush LE & John DT. Intranasal immunization of mice against *Naegleria fowleri*. *J Protozool* 1988; 35: 172–176.
- 26) Ferrante A. Free-living amoebae: pathogenicity and immunity. *Parasite Immunol* 1991; 13: 31–47.
- 27) hong YH, Ferrante A, Rowan-Kelly B & O'Keefe D. Immunization with live amoebae, amoebic lysate and culture supernatant in experimental *Naegleria meningoencephalitis*. *Trans R Soc Trop Med Hyg* 1980; 74: 570–576.
- 28) Naveed, S., Abbas, S.S., Qamar, F., Ali, Z.B., Kiran, S. and Zehra, S. (2015) Textaphrenia; Turmoil for Adults. *World Journal of Pharmaceutical and Life Sciences*, 1, 70-72
- 29) Safila Naveed, Fatima Qamar, Syeda Sarah Abbas, Syeda Zainab Manahil Khalid, Javeria Idrees, Sadia Safdar, Haniyah Mansoor, Sana Sohail. Rationality of Antibiotic Use A Survey Report. *Journal of Biotechnology and Biosafety*. 3(4):282-287.
- 30) Naveed, S., Qamar, F., Abbas, S.S., Jawed, S.H., Raza, W., Khan, M. and Iqbal, B. (2015) Appraisal of Techniques, Investigation and Analysis of Vitamin (B7) Biotin. *Open Access Library Journal*, 2: e1894. <http://dx.doi.org/10.4236/oalib.1101894>
- 31) Abbas SS, Qamar F, Naveed S (2015) Pharmacy: A Dignified Profession but yet Deserted; A Dilemma for Pharmacy Profession and Future Pharmacist. *J Bioequiv Availab* 7: e65. doi:10.4172/jbb.10000e65
- 32) Naveed, S., Qamar, F., Abbas, S.S., Jawed, S.H., Raza, W., Khan, M. and Iqbal, B. (2015) Appraisal of Techniques, Investigation and Analysis of Vitamin (B7) Biotin. *Open Access Library Journal*, 2: e1894. <http://dx.doi.org/10.4236/oalib.1101894>
- 33) Naveed S, Sana A, Rehman H, Qamar F, Abbas SS, et al. (2015) Prevalence and Consequences of PHOBIAS, Survey Based Study in Karachi. *J Bioequiv Availab* 7: 140-143. doi:10.4172/jbb.1000228
- 34) Safila Naveed, Fatima Qamar, Syeda Sarah Abbas, Sehrish Batool and Syeda Zainab (2015). Availability of Different Brands of Atenolol In Different Medium Using Uv Spectrophotometer. *Journal of Biotechnology and Biosafety*. 3(2): 203-208.
- 35) Safila Naveed, Fatima Qamar, Syeda Sarah Abbas, Sehrish Batool, Syed Hameez Jawed & Syeda Zainab. Accessibility of Altered Trade Names of Ranitidine in different standard by UV Spectrophotometric Technique. *Journal of Biotechnology Biosafety*. 3(2):209-213
- 36) Syeda Sarah Abbas, Safila Naveed, Fatima Qamar, Syeda Zainab, Syed Hameez Jawed, Sehrish Kiran, Sania Zehra, Zohra Barkat Ali. Autism Spectrum Disorder (ASD); A Threat to Social Communication. *wjpls*, 2015, Vol. 1, Issue 1, 203-205